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TITLE OF THE INVENTION

GAMMA-CONOPEPTIDES

ABSTRACT OF THE DISCLOSURE

This invention relates to relatively short peptides about 25-40 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogs to the naturally available peptides, and which include three cyclizing disulfide linkages and one or more γ -carboxyglutamate residues. More specifically, the present invention is directed to γ -conopeptides having the general formula I: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Cys-Cys-Xaa₅-Cys-Xaa₆-Cys-Xaa₇ (SEQ ID NO:1), as described herein; or having the general formula II: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Cys-Cys-Xaa₅-Xaa₆-Cys-Xaa₇-Cys-Xaa₈ (SEQ ID NO:2), as defined herein; or having the general formula III: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Xaa₅-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Xaa₆-Cys-Xaa₇ (SEQ ID NO:3), as described herein; or having the general formula IV: Xaa₁-Cys-Xaa₂-Cys-Xaa₃-Xaa₄-Xaa₅-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Xaa₆-Cys-Xaa₇ (SEQ ID NO:4), as described herein; or having the general formula V: Xaa₁-Xaa₂-Cys-Xaa₃-Xaa₄-Phe-Xaa₅-Cys-Thr-Xaa₆-Ser-Xaa₇-Cys-Cys-Ser-Asn-Ser-Cys-Asp-Gln-Thr-Tyr-Cys-Xaa₈-Leu-Xaa₉ (SEQ ID NO:5), as described herein. The invention further relates to specific γ -conopeptides, specific pro- γ -conopeptides and nucleic acids encoding the pro- γ -conopeptides. The invention also includes pharmaceutically acceptable salts of the conopeptides. These conopeptides are useful as agonists of neuronal pacemaker calcium channels.